Dr. Catherine Shu Faculty Spotlight

By Simran Shah

Class of 2027

Based on an Interview of Dr. Catherine Shu, the Price Family Associate Professor of Medicine and Director of the Thoracic Medical Oncology Service

On September 15, 2021, biopharmaceutical company Takeda Oncology announced that its breakthrough new drug, mobocertinib, was approved for Accelerated Approval by the FDA for the treatment of a specific kind of metastatic lung cancer[1]. This type of cancer is driven by a gene called EGFR that had made it nearly untreatable, and mobocertinib was a ground-breaking drug that used a brand-new mechanism to fight the disease. The building excitement in the oncology community was cut short just two years later when, on October 2, 2023, Takeda voluntarily withdrew mobocertinib from the market after its latest round of trials[2]. The drug hadn't harmed patients or revealed any new, dangerous side effects. It had simply not had as big of an effect as the researchers thought it would, and thus, could not be granted further approval.

While these results were shocking for many, they weren't surprising for Dr. Catherine Shu, a medical oncologist who specializes in the treatment and research of thoracic cancer, particularly lung cancer. Dr. Shu is a leader in lung cancer research, and she's seen mighty drugs fall before. Her key to not getting discouraged is to focus on the reward: the chance to see drugs from the early stages of development to eventually treating and curing patients in the clinic.

On Dr. Shu's pediatric oncology rotation as a medical student, she found the service emotionally challenging, but as a resident, she began to see the flipside. Dr. Shu was drawn to the life-saving treatment options that were rapidly being developed and the new ways patients with serious cancer diagnoses could be saved. She tells stories of patients who would've been beyond saving even ten years ago who can now be successfully treated and gain high-quality years back thanks to new immunotherapies.

Initially drawn in by innovation, Dr. Shu was captivated by the hope that a once refractory disease could possibly be treated by a novel drug. Once disheartened by the bleak outcomes in oncology, Dr. Shu now centers her career around conversations with patients, many facing harsh prognoses. She describes the primary goal of her career as being a compassionate physician whose patients know that she cares deeply.

She also found herself increasingly interested in lung cancer, a disease that she explains is complicated and marred by stigma. Dr. Shu's mission to fight the disease extends to pushing

back against the stereotype that lung cancer is only a smoker's disease. In fact, recent research has uncovered lung cancer's exceptional heterogeneity; there are a dozen different types of lung cancers, each with a different set of etiologies and characteristics. Among these, a quarter of lung cancers are found in people who never smoked at all, and the notoriously difficult-to-treat EGFR-driven tumors are largely found in non-smoking young women.

This new understanding is a marked shift from the 90's, brought on by the development of next-generation genetic sequencing that has identified a variety of mutations in different tumors. These discoveries have sparked new, focused areas of research and led to more targeted treatments for many kinds of lung cancers. Dr. Shu tells the story of a patient diagnosed with lung cancer at a time when her life expectancy was bleak. They tried many different treatments with limited success. The patient remained resilient, and the marginal benefits were just enough to keep her alive. Eventually, a new drug was approved that directly treated her mutation specifically, and she has been successfully on this treatment for over a year and counting.

It wasn't long into her career until Dr. Shu began taking part in clinical research herself. In her experience as a clinician, she understands that her patients depend not only on her expertise in the currently approved drugs, but also on her detailed knowledge of ongoing trials and upcoming research that could be lifesaving. To be the best provider she could be, Dr. Shu quickly realized she had to spend time out of the clinic and in the laboratory.

She now splits her time her time in half between seeing patients in the clinic and running clinical trials for new drugs, particularly a class of drugs called immunotherapies. One drug that Dr. Shu had been working on, amivantamab, targets the same EGFR-driven lung cancers that mobocertinib was designed to. On October 20, 2021, barely two weeks after Takeda Oncology withdrew mobocertinib, Dr. Shu and collaborators published promising results showing that amivantamab "yielded robust and durable responses" in patients with EGFR-driven lung cancer[3].

Amivantamab employs yet another groundbreaking mechanism. It is a bivalent antibody, meaning it works in two ways that together provide a greater treatment effect than either mechanism alone. Previous drugs had tried suppressing the mutated EGFR protein directly, but

the cancers could develop resistance to this single-pronged approach. The tumors evolved to grow through an alternative pathway using a protein called MET and were no longer treatable. Amivantamab is designed to block both EGFR and MET, treating the tumor directly and blocking it's escape path. Dr. Shu helped lead the trials to show that, in patients for whom all other known treatments had failed, amivantamab was a new source of hope.

Dr. Shu insists that her successful research career is supportive of her main goal: compassionately treat and serve each patient she sees. Her dual focus on seeing patients and conducting research echoes her latest drug: both archetypes of a rapidly evolving field that leverage a second identity to better serve their purpose.

Dr. Shu's true impact is on the lives of those she treats and is best expressed by her patients themselves. Jane Hanley was diagnosed with advanced metastatic lung cancer in early 2015 and received such harsh chemotherapy and radiation that she decided to stop treatment altogether. She was referred to Columbia University hospitals, and after meeting Dr. Shu, Jane decided to start a new immunotherapy that was still in trials[4]. Since then, Jane has been in two clinical trials over eight years with treatments that she credits with saving her life. She offers a testimony to Dr. Shu's care in an online review comment: "Dr. Shu is compassionate, caring, and exists in the top tier of medical oncologists. I was lucky to be put in this trial with her at the helm and feel it's not an exaggeration to say I owe my life to her and to this organized, well-supervised clinical trial"[5].

References:

1. *Takeda's EXKIVITYTM (mobocertinib) approved by U.S. FDA as the first oral therapy specifically designed for patients with EGFR EXON20 Insertion+ NSCLC*. Takeda Pharmaceuticals: Global Homepage. (n.d.-b). https://www.takeda.com/newsroom/newsreleases/2021/takeda-exkivity-mobocertinib-approved-by-us-fda/
2. *Takeda provides update on lung cancer program*. Takeda Pharmaceuticals: Global Homepage. (n.d.-a). https://www.takeda.com/newsroom/newsreleases/2023/Takeda-Provides-Update-on-EXKIVITY-mobocertinib/
3. Park, K., Haura, E. B., Leighl, N. B., Mitchell, P., Shu, C. A., Girard, N., Viteri, S., Han, J.-Y., Kim, S.-W., Lee, C. K., Sabari, J. K., Spira, A. I., Yang, T.-Y., Kim, D.-W., Lee, K. H., Sanborn, R. E., Trigo, J., Goto, K., Lee, J.-S., … Cho, B. C. (2021a, October 20). *Amivantamab in EGFR exon 20 insertion-mutated non-small-cell lung cancer progressing on Platinum chemotherapy: Initial results from the Chrysalis Phase I Study*. Journal of clinical oncology : official journal of the American Society of Clinical Oncology. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8791812/
4. *Jane's story: Cancer immunotherapy brings hope and healing*. Herbert Irving Comprehensive Cancer Center (HICCC) - New York. (2021, April 20). https://www.cancer.columbia.edu/patients/patient-stories/janes-story-cancer-immunotherapy-brings-hope-and-healing
5. *Dr. Catherine Shu, MD*. Healthgrades. (n.d.). https://www.healthgrades.com/physician/dr-catherine-shu-g37g3